EXAMINER'S AMENDMENT AND COMMENTS

1. In consideration of phone interview (Interview Summary of 08 July 2011, copy attached hereto), the finality of Office Action mailed 04 March 2011 has been vacated.

Accordingly, the following Office Action is issued in consideration of:

- supplemental response and amendment filed 25 October 2010 as supplement to amendment and response filed 09 August 2010; and
- amendment and response filed 09 August 2010.

2. The response and amendment to Claims filed 09 August 2010 is therefore acknowledged and entered.

3. Also acknowledged and entered is Applicants' Supplemental amendment filed 25 October 2010.

4. The Office Action that follows below is in consideration of Applicants' amendment and remarks filed on each of 09 August 2010 and 25 October 2010.

5. Examiner regrets any inconvenience because of delays in issuing the following Office Action.

Claims Status

6. According to the Supplemental amendment filed 25 October 2010, following is the Claims status:

- Claims 1-152 are cancelled;
- Claim 170 is added; and
- Claims 153-170 are pending and are examined on merits.

Withdrawals

7. In view of the Supplementary Remarks and Amendment filed 25 October 2010, and Remarks and Amendments filed 09 August 2010 to final office action mailed 12 March 2010, and in view of cancellation of Claims 1-152, the following objections and rejections in the office action mailed 22 June 2009 are moot:

- Objection to Claims 96-116 and 127-131 for lack of metes and bounds of Claims 96-98 and 127-131 and improper dependency of Claims 97-116; and

- Anticipatory rejection of Claims 96-97, 99-116 and 130 as unpatentable under 35 U.S.C. §102(b) as anticipated by Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W. B. Saunders Co., Philadelphia, 1988, Page 581).

Informals

8. The Art Unit location of instant Non-Provisional application (i.e., 09/484,886), currently under prosecution at the United States Patent and Trademark Office (i.e., USPTO) is changed to Art Unit 1653. To expedite the prosecution of the instant application (i.e., 09/484,886) and in correlating any papers for the instant application (i.e., 09/484,886), please ensure that all further correspondence regarding the instant application (i.e., 09/484,886) should be directed to Examiner Kailash C. Srivastava in Art Unit 1653.

Examiner's Amendment

9. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicants, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview on 08 July 2011 with Mr. Thomas J. Kowalski, Applicants' Representative.

In the Claims

Please amend the Claims as follows:

1-152. (Cancelled)

153. (Curremly Amended) A method for producing a substantially pure, recombinant,
glycosylated erythropoietin (EPO) that has *in vivo* activity, including stimulating erythropoiesis, comprising:

a) infecting *Spodoptera frugiperda* insect cells that grow in serum-free media with a baculovirus expression system comprising a recombinant baculovirus that comprises DNA coding for EPO such that the recombinant EPO is expressed;

b) culturing the infected insect *Spodoptera frugiperda* cells in serum-free media; and

c) purifying the recombinant EPO 10 95% or greater purity,

whereby the substantially pure, recombinant, glycosylated EPO that has *in vivo* activity of between 200,000 U/mg protein and 500,000 U/ mg protein, including stimulating erythropoiesis, is produced.

154. (Cancelled)

155. (Currently Amended) ~~The method of Claim153,~~ A method for producing substantially pure, recombinant. glycosylated eryrhropoietin (EPO) that has *in vivo* activity, including stimulating erythropoiesis, comprising: ~~wherein the insect cells are *Spodoptera frugiperda* 900+ cells.~~

a) infecting *Spodoptera frugiperda* SF900+ insect cells that grow in serum-free media with a baculovirus expression system comprising a recombinant baculovirus that comprises DNA coding for EPO such that the recombinant EPO is expressed;

b) culturing the infected *Spodoptera frugiperda* SF900+ insect cells in serum-free media; and

c) purifying the recombinant EPO to 95% or greater purity,

whereby the substantially pure recombinant, glycosylated EPO that has *in vivo* activity, including stimulating erythropoiesis, is produced.

156. ((Cancelled)

157. (Cancelled)

158. (Cancelled)

159. (Currently Amended)) ~~The method of Claim153,~~ A method for producing substantially pure, recombinant. glycosylated eryrhropoietin (EPO) that has *in vivo* activity, including stimulating erythropoiesis, comprising:

a) infecting *Spodoptera frugiperda* insect cells that grow in serum-free media with a baculovirus expression system comprising a recombinant baculovirus that comprises DNA coding for EPO such that the recombinant EPO is expressed;

b) culturing the infected *Spodoptera frugiperda* insect cells in serum-free media; and

c) purifying the recombinant EPO to 95% or greater purity, whereby the substantially pure recombinant, glycosylated EPO that has *in vivo* activity, including stimulating erythropoiesis, is produced, wherein the infecting of the insect cells with the recombinant baculovirus, the culturing of the insect cells, or both is in an apparatus for growing cells, wherein the apparatus comprises:

[[(a)]] (i) at least one bioreactor for cell culture;

[[(b)]] (ii) at least one vessel for culture media;
whereby the bioreactor and vessel are in fluid communication, and
wherein the bioreactor, vessel, or both are optionally stirred;

[[(c)]] (iii) a dialysis means for circulating culture media, cell culture, or both,
whereby there is a first cell culture loop between the bioreactor and the dialysis means and a second media replenishment loop between the vessel and the dialysis means;

[[(d)]] (iv) in-operation dialysis between the culture media and the cell culture;

[[(e)]] (v) at least one means tor delivery of oxygen comprising a hollow fiber filter oxygenator,
whereby the oxygen is delivered directly to cells in a circulating loop of cells before cell entry into the hollow fiber filter.

160. (Previously presented) The method of claim 159, wherein in the apparatus the means for delivery of oxygen comprises at least one or more of the following:

a) means for in-line sparging;

b) means for delivery of at least one oxygen-containing compound that releases dissolved oxygen into cell culture;

c) means for delivery of oxygen positioned upstream of input of circulating cell culture returning to the bioreactor;

d) means for delivery of oxygen providing an average dissolved oxygen concentration of about 60%;

e) means for delivery of oxygen providing an average dissolved oxygen concentration of greater than about 40%; and,

f) means for delivery of oxygen providing an average dissolved oxygen concentration between about 30% and about 90%, between about 40% and about 80%, or between about 50% and about 70%.

161. (Previously presented) The method of claim 159, wherein in the apparatus the means for delivery of oxygen comprises at least one or more of the following:

a) means for in-line sparging;

b) means for delivery of at least one oxygen-containing compound that releases dissolved oxygen into cell culture;

c) means for delivery of oxygen positioned upstream of input of circulating cell culture returning to the bioreactor;

162. (Previously presented) The method of claim 160, wherein in the apparatus the dialysis means comprises at least one semi-permeable membrane, at least one means for delivery of oxygen into the cell culture loop, or both.

163. (Previously presented) The method of claim 160, wherein the apparatus further comprises one or more of the following:

a) means for measuring physical parameters of the cell culture or the cell culture media;

b) means for measuring chemical parameters of the cell culture or the culture media;

c) means for measuring dissolved oxygen concentration;

d) means for measuring pH;

e) means for measuring pH and dissolved oxygen concentration;

f) means for measuring temperature;

g) means for measuring cell density or amount of cells;

h) means for adjusting physical parameters of the cell culture or the cell culture media in response to data from the measuring means;

i) means for adjusting chemical parameters of the cdl culture or the culture media in response to data from the measuring means;

j) means for adjusting dissolved oxygen concentration;

k) means tor adjusting pH;

l) means for adjusting temperature;

m) means for adjusting dissolved carbon dioxide concentration; and

n) means for adding a vector in response to a cell density or cell amount measurement.

164. (Previously presented) The method of claim 160, wherein in the apparatus pH is measured, and in response to the pH measurement, dissolved carbon dioxide concentration is adjusted.

165. (Previously presented) The method of claim 160, wherein in the apparatus dissolved oxygen concentration is measured, and in response to the dissolved oxygen measurement, the dissolved oxygen concentration is adjusted.

166. (Previously presented) The method of claim 160, wherein in the apparatus dissolved oxygen concentration is measured, pH is set to a desired level, and carbon dioxide is adjusted when pH varies from the desired level, whereby the dissolved oxygen concentration varies periodically as a function of time.

167. (Previously presented) The method of claim 160, wherein in the apparatus the dissolved oxygen concentration is measured, and the measurement varies from 30% to 90%, from 40% to 80%, from 50% to 70%, or averages about 60%.

168. (Previously presented) The method of claim 160, wherein in the apparatus the dissolved oxygen concentration is measured, and the measurement varies from high value to low value over about 10 to about 30 minutes , or over about 20 minutes.

169. (Previously presented) The method of claim 160, wherein in the apparatus the dissolved oxygen concentration is measured, and a plot of the dissolved oxygen concentration measurement as a function of time comprises a sin wave.

170. (Currently Amended) Substantially pure, recombinant. glycosylated EPO produced by a method as recited in anyone of claims 153, 155, [[157]] or 159-169.

Conclusion

10. Claims 153, 155 and 159-170 are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:00 A.M. to 5:30 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sue X. Liu can be reached at (571)-272-5539 Monday through Friday 9:00 A.M. to 4:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e.,

PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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